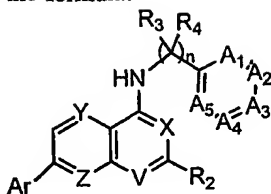


What is claimed is:

1. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR<sub>1</sub>, such that at least one of V and X is N;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

R<sub>2</sub> is:

(i) halogen, nitro or cyano; or

(ii) a group of the formula -R<sub>x</sub>-L-M-R<sub>y</sub>, wherein:

R<sub>x</sub> is C<sub>1</sub>-C<sub>3</sub>alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>2</sub>), N(R<sub>2</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>2</sub>) or N(R<sub>2</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond, C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl or C<sub>1</sub>-C<sub>8</sub>alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

R<sub>y</sub> is:

(a) hydrogen;

(b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)amino, C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

(c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and

R<sub>z</sub> is:

(a) hydrogen;

(b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

(c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

n is 1, 2 or 3;

Each R<sub>3</sub> is independently:

(i) chosen from hydrogen, cyano and C<sub>1</sub>-C<sub>4</sub>alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;

- (ii) taken together with R<sub>4</sub> attached to the same carbon atom to form an oxo group;
  - (iii) taken together with R<sub>4</sub> attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
  - (iv) taken together with a second R<sub>3</sub> group to form a 3- to 7-membered carbocycle; or
  - (v) taken together with A<sub>1</sub> to form a fused 5- to 7-membered carbocycle or heterocycle;
- wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C<sub>1</sub>-C<sub>4</sub>alkyl and haloC<sub>1</sub>-C<sub>4</sub>alkyl;

Each R<sub>4</sub> is:

- (i) independently chosen from hydrogen, cyano and C<sub>1</sub>-C<sub>4</sub>alkyl; or
- (ii) taken together with R<sub>3</sub> attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R<sub>b</sub>;

A<sub>1</sub> is N or CR<sub>a</sub>, or A<sub>1</sub> is taken together with a R<sub>3</sub> group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A<sub>2</sub>, A<sub>3</sub>, A<sub>4</sub> and A<sub>5</sub> are independently N or CR<sub>a</sub>;

R<sub>a</sub> is independently chosen at each occurrence from hydrogen, R<sub>b</sub> and groups that are taken together with an adjacent R<sub>a</sub> to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from:

- (i) hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH; and
- (ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl, C<sub>1</sub>-C<sub>8</sub>alkynyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>4</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>8</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>8</sub>alkyl)aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino.

2. A compound or salt according to claim 1, wherein Ar is phenyl or pyridyl, each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, COOH, aminocarbonyl, aminosulfonyl, cyano, nitro, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkenyl, C<sub>1</sub>-C<sub>4</sub>alkynyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, haloC<sub>1</sub>-C<sub>4</sub>alkoxy, C<sub>1</sub>-C<sub>4</sub>alkanoyl, C<sub>1</sub>-C<sub>4</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl

3. A compound or salt according to claim 2, wherein Ar is phenyl or 2-pyridyl, each of which is substituted with from 1 to 3 substituents independently chosen from halogen, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy and haloC<sub>1</sub>-C<sub>6</sub>alkoxy.

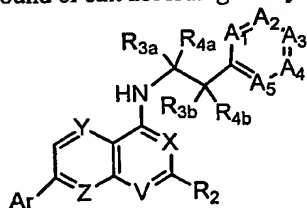
4. A compound or salt according to claim 3, wherein at least one substituent of Ar is located *ortho* to the point of attachment.

5. A compound or salt according to claim 4, wherein Ar is mono-substituted 2-pyridyl, wherein the substituent is halogen, trifluoromethyl or methyl.

6. A compound or salt according to any one of claims 1-5, wherein X and V are N.

7. A compound or salt according to claim 6, wherein Y is CH.

8. A compound or salt according to any one of claims 1-7, having the formula:



wherein:

R<sub>3a</sub> is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with R<sub>4a</sub> to form an oxo group; or
- (iii) taken together with R<sub>4a</sub> or R<sub>3b</sub> to form a 3- to 5-membered carbocycle;

R<sub>3b</sub> is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with R<sub>4b</sub> to form an oxo group;
- (iii) taken together with R<sub>4b</sub> or R<sub>3a</sub> to form a 3- to 5-membered carbocycle; or
- (iv) taken together with A<sub>1</sub> to form a fused 5- to 7-membered carbocycle;

R<sub>4a</sub> is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with R<sub>3a</sub> to form an oxo group or a 3- to 5-membered carbocycle; and

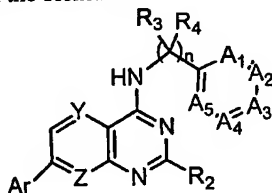
R<sub>4b</sub> is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with R<sub>3b</sub> to form an oxo group or a 3- to 5-membered carbocycle.

9. A compound or salt according to claim 8, wherein each of R<sub>3a</sub>, R<sub>3b</sub>, R<sub>4a</sub> and R<sub>4b</sub> is hydrogen.

10. A compound or salt according to claim 8, wherein R<sub>3a</sub>, R<sub>4a</sub> and R<sub>4b</sub> are hydrogen, and R<sub>3b</sub> is methyl or taken together with A<sub>1</sub> to form a fused cyclopentyl group.

11. A compound or salt according to claim 8, wherein either:  
 $R_{3a}$  and  $R_{4a}$  are taken together to form an oxo group, and  $R_{3b}$  and  $R_{4b}$  are both hydrogen; or  
 $R_{3b}$  and  $R_{4b}$  are taken together to form an oxo group, and  $R_{3a}$  and  $R_{4a}$  are both hydrogen.
12. A compound or salt according to any one of claims 1-11, wherein:  
 $A_1$  is  $CR_a$ , or  $A_1$  is taken together with a  $R_3$  group to form a fused cyclopentyl or cyclohexyl group;  
 $A_2$ ,  $A_3$  and  $A_4$  are independently  $CR_a$ ;  
 $A_5$  is N or  $CR_a$ ; and  
 $R_a$  is independently chosen at each occurrence from hydrogen, halogen, cyano,  $C_1$ - $C_6$ alkyl, ( $C_3$ - $C_8$ cycloalkyl) $C_0$ - $C_4$ alkyl, halo $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy, halo $C_1$ - $C_6$ alkoxy,  $C_2$ - $C_4$ alkyl ether,  $C_1$ - $C_4$ alkanoyl,  $C_1$ - $C_6$ alkylsulfonyl, aminosulfonyl, mono- and di-( $C_1$ - $C_6$ alkyl)aminosulfonyl, and mono- and di-( $C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl.
13. A compound or salt according to claim 12, wherein at least one  $R_a$  is not hydrogen.
14. A compound or salt according to claim 13, wherein  $R_a$  is independently chosen at each occurrence from hydrogen, halogen, cyano, methyl, ethyl, trifluoromethyl, methoxy and ethoxy.
15. A compound or salt according to any one of claims 1-14, wherein  $R_2$  is  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkenyl,  $C_2$ - $C_6$ alkyl ether, mono- or di-( $C_1$ - $C_6$ alkyl)amino $C_1$ - $C_6$ alkyl, mono- or di-( $C_1$ - $C_6$ alkenyl)amino $C_1$ - $C_6$ alkyl, ( $C_4$ - $C_{10}$ carbocycle) $C_1$ - $C_6$ alkyl, (4- to 10-membered heterocycle) $C_1$ - $C_6$ alkyl, mono- or di-( $C_1$ - $C_6$ alkyl)amino $C_2$ - $C_6$ alkyl ether, ( $C_4$ - $C_{10}$ carbocycle) $C_2$ - $C_6$ alkyl ether or (4- to 10-membered heterocycle) $C_2$ - $C_6$ alkyl ether, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano,  $C_1$ - $C_4$ alkyl and halo $C_1$ - $C_4$ alkyl.
16. A compound or salt according to claim 15, wherein  $R_2$  is  $C_2$ - $C_6$ alkyl ether, mono- or di-( $C_1$ - $C_6$ alkyl)amino $C_1$ - $C_4$ alkyl, mono- or di-( $C_1$ - $C_6$ alkenyl)amino $C_1$ - $C_6$ alkyl, or (4- to 10-membered heterocycloalkyl) $C_1$ - $C_4$ alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano,  $C_1$ - $C_4$ alkyl and halo $C_1$ - $C_4$ alkyl.
17. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

Y and Z are each independently N or  $CR_1$ ;

$R_1$  is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino,  $C_1$ - $C_6$ alkyl, halo $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy, halo $C_1$ - $C_6$ alkoxy and mono- and di-( $C_1$ - $C_6$ alkyl)amino;

$R_2$  is:

- (i) hydrogen, halogen, nitro or cyano; or  
 (ii) a group of the formula  $-R_x-L-M-R_y$ , wherein:

$R_x$  is  $C_0$ - $C_3$ alkylene;

$L$  is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S,  $SO_2$ ,  $(C=O)_pN(R_z)$ ,  $N(R_z)(C=O)_p$ ,  $SO_2N(R_z)$  or  $N(R_z)SO_2$ , wherein  $p$  is 0 or 1;

$M$  is a single covalent bond,  $C_1$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkenyl or  $C_1$ - $C_8$ alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

$R_y$  is:

- (a) hydrogen;
- (b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl,  $C_1$ - $C_8$ alkoxy,  $(C_1$ - $C_8$ alkyl)amino $C_0$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkanoyl,  $C_2$ - $C_8$ alkanone,  $C_2$ - $C_8$ alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; or
- (c) taken together with  $R_x$  or  $R_z$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

$R_z$  is:

- (a) hydrogen;
- (b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl,  $C_1$ - $C_8$ alkanoyl,  $C_2$ - $C_8$ alkanone,  $C_2$ - $C_8$ alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; or
- (c) taken together with  $R_x$  or  $R_y$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

$n$  is 1, 2 or 3;

Each  $R_3$  is independently:

- (i) chosen from hydrogen, cyano and  $C_1$ - $C_4$ alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
  - (ii) taken together with  $R_4$  attached to the same carbon atom to form an oxo group;
  - (iii) taken together with  $R_4$  attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
  - (iv) taken together with a second  $R_3$  group to form a 3- to 7-membered carbocycle; or
  - (v) taken together with  $A_1$  to form a fused 5- to 7-membered carbocycle or heterocycle;
- wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy,  $C_1$ - $C_4$ alkyl and halo $C_1$ - $C_4$ alkyl;

Each  $R_4$  is independently:

- (i) hydrogen, cyano or  $C_1$ - $C_4$ alkyl; or
- (ii) taken together with  $R_3$  attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 1 to 3 substituents independently selected from:

- (i) hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH; and
- (ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl, C<sub>1</sub>-C<sub>8</sub>alkynyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>4</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>8</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>8</sub>alkyl)aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino;

A<sub>1</sub> is N or CR<sub>a</sub>, or A<sub>1</sub> is taken together with a R<sub>3</sub> group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A<sub>2</sub>, A<sub>3</sub>, A<sub>4</sub> and A<sub>5</sub> are independently N or CR<sub>a</sub>;

R<sub>a</sub> is independently chosen at each occurrence from hydrogen, R<sub>b</sub> and groups that are taken together with an adjacent R<sub>a</sub> to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from:

- (i) hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH; and
- (ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl, C<sub>1</sub>-C<sub>8</sub>alkynyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>4</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>8</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>8</sub>alkyl)aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino.

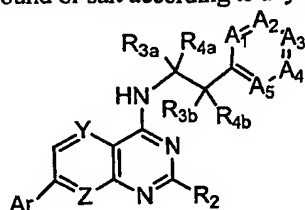
18. A compound or salt according to claim 17, wherein Ar is phenyl or pyridyl, each of which is substituted with from 1 to 3 substituents independently chosen from hydroxy, halogen, amino, COOH, aminocarbonyl, aminosulfonyl, cyano, nitro, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkenyl, C<sub>1</sub>-C<sub>4</sub>alkynyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkoxy, C<sub>1</sub>-C<sub>4</sub>alkanoyl, C<sub>1</sub>-C<sub>4</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl.

19. A compound or salt according to claim 18, wherein at least one substituent of Ar is located *ortho* to the point of attachment.

20. A compound or salt according to claim 19, wherein Ar is mono-substituted 2-pyridyl, wherein the substituent is halogen, trifluoromethyl or methyl.

21. A compound or salt according to any one of claims 17-20, wherein Y is CH.

22. A compound or salt according to any one of claims 17-21, having the formula:



wherein:

R<sub>3a</sub> is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with R<sub>4a</sub> to form an oxo group; or
- (iii) taken together with R<sub>4a</sub> or R<sub>3b</sub> to form a 3- to 5-membered carbocycle;

R<sub>3b</sub> is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with R<sub>4b</sub> to form an oxo group;
- (iii) taken together with R<sub>4b</sub> or R<sub>3a</sub> to form a 3- to 5-membered carbocycle; or
- (iv) taken together with A<sub>1</sub> to form a fused 5- to 7-membered carbocycle;

R<sub>4a</sub> is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with R<sub>3a</sub> to form an oxo group or a 3- to 5-membered carbocycle; and

R<sub>4b</sub> is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with R<sub>3b</sub> to form an oxo group or a 3- to 5-membered carbocycle.

23. A compound or salt according to claim 22, wherein each of R<sub>3b</sub>, R<sub>3a</sub>, R<sub>4a</sub> and R<sub>4b</sub> is hydrogen.

24. A compound or salt according to claim 22, wherein R<sub>3b</sub>, R<sub>4a</sub> and R<sub>4b</sub> are hydrogen, and R<sub>3a</sub> is methyl or taken together with A<sub>1</sub> to form a fused cyclopentyl group.

25. A compound or salt according to claim 22, wherein either:

R<sub>3a</sub> and R<sub>4a</sub> are taken together to form an oxo group, and R<sub>3b</sub> and R<sub>4b</sub> are both hydrogen; or  
 R<sub>3b</sub> and R<sub>4b</sub> are taken together to form an oxo group, and R<sub>3a</sub> and R<sub>4a</sub> are both hydrogen.

26. A compound or salt according to any one of claims 17-25, wherein:

A<sub>1</sub> is CR<sub>n</sub>, or A<sub>1</sub> is taken together with a R<sub>3</sub> group to form a fused cyclopentyl or cyclohexyl group;

A<sub>2</sub>, A<sub>3</sub> and A<sub>4</sub> are independently CR<sub>n</sub>;

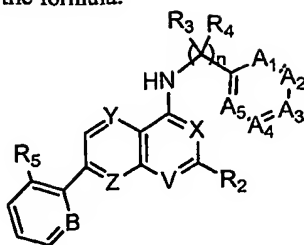
A<sub>5</sub> is N or CR<sub>n</sub>; and

R<sub>n</sub> is independently chosen at each occurrence from hydrogen, halogen, cyano, C<sub>1</sub>-C<sub>6</sub>alkyl, (C<sub>3</sub>-C<sub>8</sub>cycloalkyl)C<sub>0</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy, C<sub>2</sub>-C<sub>4</sub>alkyl ether, C<sub>1</sub>-C<sub>4</sub>alkanoyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl.

27. A compound or salt according to claim 26, wherein at least one  $R_a$  is not hydrogen.
28. A compound or salt according to claim 27, wherein  $R_a$  is independently chosen at each occurrence from hydrogen, halogen, cyano, methyl, ethyl, trifluoromethyl, methoxy and ethoxy.
29. A compound or salt according to any one of claims 17-28, wherein  $R_2$  is:
- (i) halogen, nitro or cyano; or
  - (ii) a group of the formula  $-R_x-L-M-R_y$ , wherein:
    - $R_x$  is  $C_1$ - $C_3$ alkylene;
    - $L$  is a single covalent bond, O, (C=O), (C=O)O, O(C=O), (C=O) $_p$ N( $R_z$ ) or N( $R_z$ )(C=O) $_p$ , wherein  $p$  is 0 or 1;
    - $M$  is a single covalent bond or  $C_1$ - $C_8$ alkylene that substituted with from 0 to 4 substituents independently selected from  $R_b$ ;
    - $R_y$  is:
      - (a) hydrogen;
      - (b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl,  $C_1$ - $C_8$ alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 4 substituents independently selected from  $R_b$ ; or
      - (c) taken together with  $R_z$  to form a 4- to 10-membered heterocycle that is substituted with from 0 to 4 substituents independently selected from  $R_b$ ; and
    - $R_z$  is:
      - (a) hydrogen;
      - (b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 4 substituents independently selected from  $R_b$ ; or
      - (c) taken together with  $R_y$  to form a 4- to 10-membered heterocycle that is substituted with from 0 to 4 substituents independently selected from  $R_b$ .
30. A compound or salt according to any one of claims 17-28, wherein  $R_2$  is hydrogen,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkenyl,  $C_2$ - $C_6$ alkyl ether, mono- or di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>1</sub>-C<sub>6</sub>alkyl, mono- or di-(C<sub>1</sub>-C<sub>6</sub>alkenyl)aminoC<sub>1</sub>-C<sub>6</sub>alkyl, (C<sub>4</sub>-C<sub>10</sub> carbocycle)C<sub>1</sub>-C<sub>6</sub>alkyl, (4- to 10-membered heterocycle)C<sub>1</sub>-C<sub>6</sub>alkyl, mono- or di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>2</sub>-C<sub>6</sub>alkyl ether, (C<sub>4</sub>-C<sub>10</sub> carbocycle)C<sub>2</sub>-C<sub>6</sub>alkyl ether, or (4- to 10-membered heterocycle)C<sub>2</sub>-C<sub>6</sub>alkyl ether, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano,  $C_1$ -C<sub>4</sub>alkyl and haloC<sub>1</sub>-C<sub>4</sub>alkyl.
31. A compound or salt according to claim 30, wherein  $R_2$  is  $C_2$ -C<sub>6</sub>alkyl ether, mono- or di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>1</sub>-C<sub>4</sub>alkyl, mono- or di-(C<sub>1</sub>-C<sub>6</sub>alkenyl)aminoC<sub>1</sub>-C<sub>6</sub>alkyl, or (4- to 10-membered heterocycloalkyl)C<sub>1</sub>-C<sub>4</sub>alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano,  $C_1$ -C<sub>4</sub>alkyl and haloC<sub>1</sub>-C<sub>4</sub>alkyl.



32. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

Y and Z are each independently N or CR<sub>1</sub>;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

B is CH or N;

R<sub>5</sub> is hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkenyl, C<sub>1</sub>-C<sub>4</sub>alkynyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, haloC<sub>1</sub>-C<sub>4</sub>alkoxy, C<sub>1</sub>-C<sub>4</sub>alkanoyl, C<sub>1</sub>-C<sub>4</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl;

R<sub>2</sub> is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R<sub>x</sub>-L-M-R<sub>y</sub>, wherein:

R<sub>x</sub> is C<sub>0</sub>-C<sub>3</sub>alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>), N(R<sub>z</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>z</sub>) or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond, C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl or C<sub>1</sub>-C<sub>8</sub>alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and

R<sub>y</sub> is:

(a) hydrogen;

(b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

(c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

R<sub>z</sub> is:

(a) hydrogen;

(b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

- (c) taken together with  $R_x$  or  $R_y$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

$n$  is 1, 2 or 3;

Each  $R_3$  is independently:

- (i) chosen from hydrogen, cyano and  $C_1$ - $C_4$ alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
  - (ii) taken together with  $R_4$  attached to the same carbon atom to form an oxo group;
  - (iii) taken together with  $R_4$  attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
  - (iv) taken together with a second  $R_3$  group to form a 3- to 7-membered carbocycle; or
  - (v) taken together with  $A_1$  to form a fused 5- to 7-membered carbocycle or heterocycle;
- wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy,  $C_1$ - $C_4$ alkyl and halo $C_1$ - $C_4$ alkyl;

Each  $R_4$  is independently:

- (i) hydrogen, cyano or  $C_1$ - $C_4$ alkyl; or
- (ii) taken together with  $R_3$  attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

$A_1$  is N or  $CR_a$ , or  $A_1$  is taken together with a  $R_3$  group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

$A_2$ ,  $A_3$ ,  $A_4$  and  $A_5$  are independently N or  $CR_a$ ;

$R_a$  is independently chosen at each occurrence from hydrogen,  $R_b$  and groups that are taken together with an adjacent  $R_a$  to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from  $R_b$ ; and

$R_b$  is independently chosen at each occurrence from:

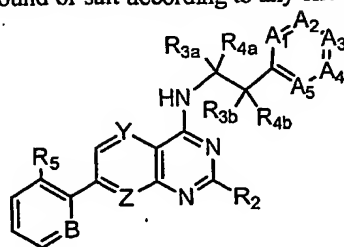
- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and  $-COOH$ ; and
- (ii)  $C_1$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkenyl,  $C_1$ - $C_8$ alkynyl, halo $C_1$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkoxy, halo $C_1$ - $C_8$ alkoxy,  $C_1$ - $C_8$ alkanoyl,  $C_3$ - $C_8$ alkanone,  $C_1$ - $C_8$ alkanoyloxy,  $C_1$ - $C_8$ alkylthio,  $C_2$ - $C_8$ alkyl ether,  $C_1$ - $C_4$ alkoxycarbonyl,  $C_1$ - $C_6$ alkylsulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)aminosulfonyl, and mono- and di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano,  $C_1$ - $C_4$ alkyl,  $C_1$ - $C_4$ alkoxy, hydroxy $C_1$ - $C_4$ alkyl, halo $C_1$ - $C_4$ alkyl, and mono- and di- $(C_1$ - $C_4$ alkyl)amino.

33. A compound or salt according to claim 32, wherein  $R_3$  is halogen, trifluoromethyl or methyl.

34. A compound or salt according to claim 32 or claim 33, wherein X and V are N.

35. A compound or salt according to claim 34, wherein Y is CH.

36. A compound or salt according to any one of claims 32-35, having the formula:



wherein:

$R_{3a}$  is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with  $R_{4a}$  to form an oxo group; or
- (iii) taken together with  $R_{4a}$  or  $R_{3b}$  to form a 3- to 5-membered carbocycle;

$R_{3b}$  is:

- (i) hydrogen, cyano, methyl or ethyl;
- (ii) taken together with  $R_{4b}$  to form an oxo group;
- (iii) taken together with  $R_{4b}$  or  $R_{3a}$  to form a 3- to 5-membered carbocycle; or
- (iv) taken together with  $A_1$  to form a fused 5- to 7-membered carbocycle;

$R_{4a}$  is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with  $R_{3a}$  to form an oxo group or a 3- to 5-membered carbocycle; and

$R_{4b}$  is:

- (i) hydrogen, methyl or ethyl; or
- (ii) taken together with  $R_{3b}$  to form an oxo group or a 3- to 5-membered carbocycle.

37. A compound or salt according to claim 36, wherein each of  $R_{3a}$ ,  $R_{3b}$ ,  $R_{4a}$  and  $R_{4b}$  is hydrogen.

38. A compound or salt according to claim 36, wherein  $R_{3a}$ ,  $R_{4a}$  and  $R_{4b}$  are hydrogen, and  $R_{3b}$  is methyl or taken together with  $A_1$  to form a fused cyclopentyl group.

39. A compound or salt according to claim 36, wherein either:

- $R_{3a}$  and  $R_{4a}$  are taken together to form an oxo group, and  $R_{3b}$  and  $R_{4b}$  are both hydrogen; or
- $R_{3b}$  and  $R_{4b}$  are taken together to form an oxo group, and  $R_{3a}$  and  $R_{4a}$  are both hydrogen.

40. A compound or salt according to any one of claims 32-39, wherein:

- $A_1$  is  $CR_n$ , or  $A_1$  is taken together with a  $R_3$  group to form a fused cyclopentyl or cyclohexyl group;
- $A_2$ ,  $A_3$  and  $A_4$  are independently  $CR_n$ ;
- $A_5$  is N or  $CR_n$ ; and

$R_a$  is independently chosen at each occurrence from hydrogen, halogen, cyano,  $C_1$ - $C_6$ alkyl, ( $C_3$ - $C_8$ cycloalkyl) $C_0$ - $C_4$ alkyl, halo $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy, halo $C_1$ - $C_6$ alkoxy,  $C_2$ - $C_4$ alkyl ether,  $C_1$ - $C_4$ alkanoyl,  $C_1$ - $C_6$ alkylsulfonyl, and mono- and di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl.

41. A compound or salt according to claim 40, wherein at least one  $R_a$  is not hydrogen.

42. A compound or salt according to claim 41, wherein  $R_a$  is independently chosen at each occurrence from hydrogen, halogen, cyano, methyl, ethyl, trifluoromethyl, methoxy and ethoxy.

43. A compound or salt according to any one of claims 32-42, wherein  $R_2$  is:

(i) halogen, nitro or cyano; or

(ii) a group of the formula  $-R_x-L-M-R_y$ , wherein:

$R_x$  is  $C_1$ - $C_3$ alkylene;

$L$  is a single covalent bond, O,  $(C=O)$ ,  $(C=O)O$ ,  $O(C=O)$ ,  $(C=O)_pN(R_z)$  or  $N(R_z)(C=O)_p$ ,  
wherein  $p$  is 0 or 1;

$M$  is a single covalent bond or  $C_1$ - $C_8$ alkylene that substituted with from 0 to 4 substituents independently selected from  $R_b$ ;

$R_y$  is:

(a) hydrogen;

(b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl,  $C_1$ - $C_8$ alkoxy,  $(C_1$ - $C_8$ alkyl)amino $C_0$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkanoyl,  $C_2$ - $C_8$ alkanone,  $C_2$ - $C_8$ alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 4 substituents independently selected from  $R_b$ ; or

(c) taken together with  $R_z$  to form a 4- to 10-membered heterocycle that is substituted with from 0 to 4 substituents independently selected from  $R_b$ ; and

$R_z$  is:

(a) hydrogen;

(b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 4 substituents independently selected from  $R_b$ ; or

(c) taken together with  $R_y$  to form a 4- to 10-membered heterocycle that is substituted with from 0 to 4 substituents independently selected from  $R_b$ .

44. A compound or salt according to any one of claims 32-42, wherein  $R_2$  is hydrogen,  $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkenyl,  $C_2$ - $C_6$ alkyl ether, mono- or di- $(C_1$ - $C_6$ alkyl)amino $C_1$ - $C_6$ alkyl, mono- or di- $(C_1$ - $C_6$ alkenyl)amino $C_1$ - $C_6$ alkyl,  $(C_4$ - $C_{10}$  carbocycle) $C_1$ - $C_6$ alkyl, (4- to 10-membered heterocycle) $C_1$ - $C_6$ alkyl, mono- or di- $(C_1$ - $C_6$ alkyl)amino $C_2$ - $C_6$ alkyl ether,  $(C_4$ - $C_{10}$  carbocycle) $C_2$ - $C_6$ alkyl ether, or (4- to 10-membered heterocycle) $C_2$ - $C_6$ alkyl ether, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano,  $C_1$ - $C_4$ alkyl and halo $C_1$ - $C_4$ alkyl.

45. A compound or salt according to claim 44, wherein  $R_2$  is  $C_2$ - $C_6$ alkyl ether, mono- or di- $(C_1$ - $C_6$ alkyl)amino $C_1$ - $C_4$ alkyl, mono- or di- $(C_1$ - $C_6$ alkenyl)amino $C_1$ - $C_6$ alkyl, or (4- to 10-membered heterocycloalkyl) $C_1$ - $C_4$ alkyl, each of which is substituted with from 0 to 4 substituents independently chosen from halogen, cyano,  $C_1$ - $C_4$ alkyl and halo $C_1$ - $C_4$ alkyl.

46. A compound or salt according to any one of claims 1-45, wherein the compound exhibits no detectable agonist activity in an *in vitro* assay of capsaicin receptor agonism.

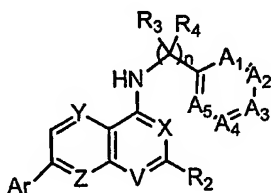
47. A compound or salt according to any one of claims 1-45, wherein the compound has an  $IC_{50}$  value of 100 nanomolar or less in a capsaicin receptor calcium mobilization assay.

48. A compound or salt according to any one of claims 1-45, wherein the compound has an  $IC_{50}$  value of 10 nanomolar or less in a capsaicin receptor calcium mobilization assay.

49. A pharmaceutical composition, comprising at least one compound or salt according to any one of claims 1-45, in combination with a physiologically acceptable carrier or excipient.

50. A pharmaceutical composition according to claim 49 wherein the composition is formulated as an injectible fluid, an aerosol, a cream, a gel, a pill, a capsule, a syrup or a transdermal patch.

51. A method for reducing calcium conductance of a cellular capsaicin receptor, comprising contacting a cell expressing a capsaicin receptor with at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or  $CR_1$ , such that at least one of V and X is N;

$R_1$  is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino,  $C_1$ - $C_6$ alkyl, halo $C_1$ - $C_6$ alkyl,  $C_1$ - $C_6$ alkoxy, halo $C_1$ - $C_6$ alkoxy and mono- and di- $(C_1$ - $C_6$ alkyl)amino;

$R_2$  is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula  $-R_x-L-M-R_y$ , wherein:

$R_x$  is  $C_0$ - $C_3$ alkylene;

L is a single covalent bond, O,  $(C=O)$ ,  $(C=O)O$ ,  $O(C=O)$ , S,  $SO_2$ ,  $(C=O)_pN(R_2)$ ,  $N(R_2)(C=O)_p$ ,  $SO_2N(R_2)$  or  $N(R_2)SO_2$ , wherein p is 0 or 1;

M is a single covalent bond, C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl or C<sub>1</sub>-C<sub>8</sub>alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and

R<sub>y</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

R<sub>z</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

n is 1, 2 or 3;

Each R<sub>3</sub> is independently:

- (i) chosen from hydrogen, cyano and C<sub>1</sub>-C<sub>4</sub>alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
  - (ii) taken together with R<sub>4</sub> attached to the same carbon atom to form an oxo group;
  - (iii) taken together with R<sub>4</sub> attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
  - (iv) taken together with a second R<sub>3</sub> group to form a 3- to 7-membered carbocycle; or
  - (v) taken together with A<sub>1</sub> to form a fused 5- to 7-membered carbocycle or heterocycle;
- wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C<sub>1</sub>-C<sub>4</sub>alkyl and haloC<sub>1</sub>-C<sub>4</sub>alkyl;

Each R<sub>4</sub> is independently:

- (i) hydrogen, cyano or C<sub>1</sub>-C<sub>4</sub>alkyl; or
- (ii) taken together with R<sub>3</sub> attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R<sub>b</sub>;

A<sub>1</sub> is N or CR<sub>a</sub>, or A<sub>1</sub> is taken together with a R<sub>3</sub> group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A<sub>2</sub>, A<sub>3</sub>, A<sub>4</sub> and A<sub>5</sub> are independently N or CR<sub>a</sub>;

R<sub>a</sub> is independently chosen at each occurrence from hydrogen, R<sub>b</sub> and groups that are taken together with an adjacent R<sub>a</sub> to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from:

(i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH; and

(ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl, C<sub>1</sub>-C<sub>8</sub>alkynyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>4</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino;

and thereby reducing calcium conductance of the capsaicin receptor.

52. A method according to claim 51, wherein the compound is a compound according to claim any one of claims 1-45.

53. A method according to claim 51, wherein the cell is contacted *in vivo* in an animal.

54. A method according to claim 53, wherein the cell is a neuronal cell.

55. A method according to claim 53, wherein the cell is a urothelial cell.

56. A method according to claim 55, wherein during contact the compound is present within a body fluid of the animal.

57. A method according to claim 56, wherein the compound is present in the blood of the animal at a concentration of 1 micromolar or less.

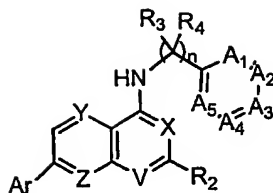
58. A method according to claim 57, wherein the compound is present in the blood of the animal at a concentration of 500 nanomolar or less.

59. A method according to claim 57, wherein the compound is present in the blood of the animal at a concentration of 100 nanomolar or less.

60. A method according to claim 53, wherein the animal is a human.

61. A method according to claim 53, wherein the compound is administered orally.

62. A method for inhibiting binding of vanilloid ligand to a capsaicin receptor *in vitro*, the method comprising contacting capsaicin receptor with at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR<sub>1</sub>, such that at least one of V and X is N;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

R<sub>2</sub> is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R<sub>x</sub>-L-M-R<sub>y</sub>, wherein:

R<sub>x</sub> is C<sub>0</sub>-C<sub>3</sub>alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>2</sub>), N(R<sub>2</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>2</sub>) or N(R<sub>2</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond, C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl or C<sub>1</sub>-C<sub>8</sub>alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and

R<sub>y</sub> is:

(a) hydrogen;

(b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)amino, C<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

(c) taken together with R<sub>x</sub> or R<sub>2</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

R<sub>2</sub> is:

(a) hydrogen;

(b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

(c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

n is 1, 2 or 3;

Each R<sub>3</sub> is independently:

(i) chosen from hydrogen, cyano and C<sub>1</sub>-C<sub>4</sub>alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;

(ii) taken together with R<sub>4</sub> attached to the same carbon atom to form an oxo group;



- (iii) taken together with  $R_4$  attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
  - (iv) taken together with a second  $R_3$  group to form a 3- to 7-membered carbocycle; or
  - (v) taken together with  $A_1$  to form a fused 5- to 7-membered carbocycle or heterocycle;
- wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy,  $C_1$ - $C_4$ alkyl and halo $C_1$ - $C_4$ alkyl;

Each  $R_4$  is independently:

- (i) hydrogen, cyano or  $C_1$ - $C_4$ alkyl; or
- (ii) taken together with  $R_3$  attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from  $R_b$ ;

$A_1$  is N or  $CR_n$ , or  $A_1$  is taken together with a  $R_3$  group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

$A_2$ ,  $A_3$ ,  $A_4$  and  $A_5$  are independently N or  $CR_n$ ;

$R_a$  is independently chosen at each occurrence from hydrogen,  $R_b$  and groups that are taken together with an adjacent  $R_a$  to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from  $R_b$ ; and

$R_b$  is independently chosen at each occurrence from:

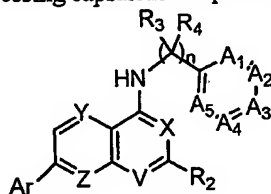
- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and  $-COOH$ ;
- and

- (ii)  $C_1$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkenyl,  $C_1$ - $C_8$ alkynyl, halo $C_1$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkoxy, halo $C_1$ - $C_8$ alkoxy,  $C_1$ - $C_8$ alkanoyl,  $C_3$ - $C_8$ alkanone,  $C_1$ - $C_8$ alkanoyloxy,  $C_1$ - $C_8$ alkylthio,  $C_2$ - $C_8$ alkyl ether,  $C_1$ - $C_4$ alkoxycarbonyl,  $C_1$ - $C_6$ alkylsulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)aminosulfonyl, and mono- and di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano,  $C_1$ - $C_4$ alkyl,  $C_1$ - $C_4$ alkoxy, hydroxy $C_1$ - $C_4$ alkyl, halo $C_1$ - $C_4$ alkyl, and mono- and di- $(C_1$ - $C_4$ alkyl)amino;

under conditions and in an amount sufficient to detectably inhibit vanilloid ligand binding to capsaicin receptor.

63. A method according to claim 62, wherein the compound is a compound according to claim any one of claims 1-45.

64. A method for inhibiting binding of vanilloid ligand to capsaicin receptor in a patient, comprising contacting cells expressing capsaicin receptor with at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR<sub>1</sub>, such that at least one of V and X is N;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

R<sub>2</sub> is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R<sub>x</sub>-L-M-R<sub>y</sub>, wherein:

R<sub>x</sub> is C<sub>0</sub>-C<sub>3</sub>alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>), N(R<sub>z</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>z</sub>) or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond, C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl or C<sub>1</sub>-C<sub>8</sub>alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and

R<sub>y</sub> is:

(a) hydrogen;

(b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

(c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

R<sub>z</sub> is:

(a) hydrogen;

(b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

(c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

n is 1, 2 or 3;

Each R<sub>3</sub> is independently:

(i) chosen from hydrogen, cyano and C<sub>1</sub>-C<sub>4</sub>alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;

- (ii) taken together with R<sub>4</sub> attached to the same carbon atom to form an oxo group;
  - (iii) taken together with R<sub>4</sub> attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
  - (iv) taken together with a second R<sub>3</sub> group to form a 3- to 7-membered carbocycle; or
  - (v) taken together with A<sub>1</sub> to form a fused 5- to 7-membered carbocycle or heterocycle;
- wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C<sub>1</sub>-C<sub>4</sub>alkyl and haloC<sub>1</sub>-C<sub>4</sub>alkyl;

Each R<sub>4</sub> is independently:

- (i) hydrogen, cyano or C<sub>1</sub>-C<sub>4</sub>alkyl; or
- (ii) taken together with R<sub>3</sub> attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R<sub>b</sub>;

A<sub>1</sub> is N or CR<sub>a</sub>, or A<sub>1</sub> is taken together with a R<sub>3</sub> group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A<sub>2</sub>, A<sub>3</sub>, A<sub>4</sub> and A<sub>5</sub> are independently N or CR<sub>a</sub>;

R<sub>a</sub> is independently chosen at each occurrence from hydrogen, R<sub>b</sub> and groups that are taken together with an adjacent R<sub>a</sub> to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH; and

- (ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl, C<sub>1</sub>-C<sub>8</sub>alkynyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>4</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino;

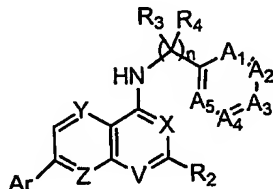
and thereby inhibiting binding of vanilloid ligand to the capsaicin receptor in the patient.

65. A method according to claim 64, wherein the compound is a compound according to claim any one of claims 1-45.

66. A method according to claim 64, wherein the patient is a human.

67. A method according to claim 64, wherein the compound is present in the blood of the patient at a concentration of 1 micromolar or less.

68. A method for treating a condition responsive to capsaicin receptor modulation in a patient, comprising administering to the patient a therapeutically effective amount of at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR<sub>1</sub>, such that at least one of V and X is N;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

R<sub>2</sub> is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R<sub>x</sub>-L-M-R<sub>y</sub>, wherein:

R<sub>x</sub> is C<sub>0</sub>-C<sub>3</sub>alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>), N(R<sub>z</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>z</sub>) or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond, C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl or C<sub>1</sub>-C<sub>8</sub>alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and

R<sub>y</sub> is:

(a) hydrogen;

(b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)amino, C<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

(c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

R<sub>z</sub> is:

(a) hydrogen;

(b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or

(c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

n is 1, 2 or 3;

Each R<sub>3</sub> is independently:

- (i) chosen from hydrogen, cyano and C<sub>1</sub>-C<sub>4</sub>alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
  - (ii) taken together with R<sub>4</sub> attached to the same carbon atom to form an oxo group;
  - (iii) taken together with R<sub>4</sub> attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
  - (iv) taken together with a second R<sub>3</sub> group to form a 3- to 7-membered carbocycle; or
  - (v) taken together with A<sub>1</sub> to form a fused 5- to 7-membered carbocycle or heterocycle;
- wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C<sub>1</sub>-C<sub>4</sub>alkyl and haloC<sub>1</sub>-C<sub>4</sub>alkyl;

Each R<sub>4</sub> is independently:

- (i) hydrogen, cyano or C<sub>1</sub>-C<sub>4</sub>alkyl; or
- (ii) taken together with R<sub>3</sub> attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R<sub>b</sub>;

A<sub>1</sub> is N or CR<sub>a</sub>, or A<sub>1</sub> is taken together with a R<sub>3</sub> group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A<sub>2</sub>, A<sub>3</sub>, A<sub>4</sub> and A<sub>5</sub> are independently N or CR<sub>a</sub>;

R<sub>a</sub> is independently chosen at each occurrence from hydrogen, R<sub>b</sub> and groups that are taken together with an adjacent R<sub>a</sub> to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH; and
- (ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl, C<sub>1</sub>-C<sub>8</sub>alkynyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>4</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino;

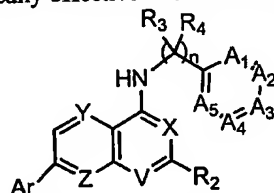
and thereby alleviating the condition in the patient.

69. A method according to claim 68, wherein the compound is a compound according to claim any one of claims 1-45.

70. A method according to claim 68, wherein the patient is suffering from (i) exposure to capsaicin, (ii) burn or irritation due to exposure to heat, (iii) burns or irritation due to exposure to light, (iv) burn, bronchoconstriction or irritation due to exposure to tear gas, air pollutants or pepper spray, or (v) burn or irritation due to exposure to acid.

71. A method according to claim 68, wherein the condition is asthma or chronic obstructive pulmonary disease.

72. A method for treating pain in a patient, comprising administering to a patient suffering from pain a therapeutically effective amount of at least one compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR<sub>1</sub>, such that at least one of V and X is N;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

R<sub>2</sub> is:

- (i) hydrogen, halogen, nitro or cyano; or
- (ii) a group of the formula -R<sub>x</sub>-L-M-R<sub>y</sub>, wherein:

R<sub>x</sub> is C<sub>0</sub>-C<sub>3</sub>alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>), N(R<sub>z</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>z</sub>) or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond, C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl or C<sub>1</sub>-C<sub>8</sub>alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and

R<sub>y</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)amino, C<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

R<sub>z</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

n is 1, 2 or 3;

Each  $R_3$  is independently:

- (i) chosen from hydrogen, cyano and  $C_1$ - $C_4$ alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
  - (ii) taken together with  $R_4$  attached to the same carbon atom to form an oxo group;
  - (iii) taken together with  $R_4$  attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
  - (iv) taken together with a second  $R_3$  group to form a 3- to 7-membered carbocycle; or
  - (v) taken together with  $A_1$  to form a fused 5- to 7-membered carbocycle or heterocycle;
- wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy,  $C_1$ - $C_4$ alkyl and halo $C_1$ - $C_4$ alkyl;

Each  $R_4$  is independently:

- (i) hydrogen, cyano or  $C_1$ - $C_4$ alkyl; or
- (ii) taken together with  $R_3$  attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from  $R_b$ ;

$A_1$  is N or  $CR_a$ , or  $A_1$  is taken together with a  $R_3$  group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

$A_2$ ,  $A_3$ ,  $A_4$  and  $A_5$  are independently N or  $CR_a$ ;

$R_a$  is independently chosen at each occurrence from hydrogen,  $R_b$  and groups that are taken together with an adjacent  $R_a$  to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from  $R_b$ ; and

$R_b$  is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and  $-COOH$ ; and
- (ii)  $C_1$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkenyl,  $C_1$ - $C_8$ alkynyl, halo $C_1$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkoxy, halo $C_1$ - $C_8$ alkoxy,  $C_1$ - $C_8$ alkanoyl,  $C_3$ - $C_8$ alkanone,  $C_1$ - $C_8$ alkanoyloxy,  $C_1$ - $C_8$ alkylthio,  $C_2$ - $C_8$ alkyl ether,  $C_1$ - $C_4$ alkoxycarbonyl,  $C_1$ - $C_6$ alkylsulfonyl, mono- and di- $(C_1$ - $C_6$ alkyl)aminosulfonyl, and mono- and di- $(C_1$ - $C_6$ alkyl)amino $C_0$ - $C_4$ alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano,  $C_1$ - $C_4$ alkyl,  $C_1$ - $C_4$ alkoxy, hydroxy $C_1$ - $C_4$ alkyl, halo $C_1$ - $C_4$ alkyl, and mono- and di- $(C_1$ - $C_4$ alkyl)amino;

and thereby alleviating pain in the patient.

73. A method according to claim 72, wherein the compound is a compound according to claim any one of claims 1-45.

74. A method according to claim 72, wherein the compound is present in the blood of the patient at a concentration of 1 micromolar or less.

75. A method according to claim 72, wherein the compound is present in the blood of the patient at a concentration of 500 nanomolar or less.

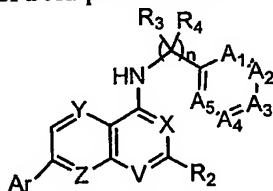
76. A method according to claim 72, wherein the compound is present in the blood of the patient at a concentration of 100 nanomolar or less.

77. A method according to claim 72, wherein the patient is suffering from neuropathic pain.

78. A method according to claim 72, wherein the pain is associated with a condition selected from: postmastectomy pain syndrome, stump pain, phantom limb pain, oral neuropathic pain, toothache, postherpetic neuralgia, diabetic neuropathy, reflex sympathetic dystrophy, trigeminal neuralgia, osteoarthritis, rheumatoid arthritis, fibromyalgia, Guillain-Barre syndrome, meralgia paresthetica, burning-mouth syndrome, bilateral peripheral neuropathy, causalgia, neuritis, neuronitis, neuralgia, AIDS-related neuropathy, MS-related neuropathy, spinal cord injury-related pain, surgery-related pain, musculoskeletal pain, back pain, headache, migraine, angina, labor, hemorrhoids, dyspepsia, Charcot's pains, intestinal gas, menstruation, cancer, venom exposure, irritable bowel syndrome, inflammatory bowel disease and trauma.

79. A method according to claim 72, wherein the patient is a human.

80. A method for treating itch in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR<sub>1</sub>, such that at least one of V and X is N;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

R<sub>2</sub> is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R<sub>x</sub>-L-M-R<sub>y</sub>, wherein:

R<sub>x</sub> is C<sub>0</sub>-C<sub>3</sub>alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>z</sub>),

N(R<sub>z</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>z</sub>) or N(R<sub>z</sub>)SO<sub>2</sub>, wherein p is 0 or 1;



M is a single covalent bond, C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl or C<sub>1</sub>-C<sub>8</sub>alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; and

R<sub>y</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)amino, C<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>z</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

R<sub>z</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

n is 1, 2 or 3;

Each R<sub>3</sub> is independently:

- (i) chosen from hydrogen, cyano and C<sub>1</sub>-C<sub>4</sub>alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
  - (ii) taken together with R<sub>4</sub> attached to the same carbon atom to form an oxo group;
  - (iii) taken together with R<sub>4</sub> attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
  - (iv) taken together with a second R<sub>3</sub> group to form a 3- to 7-membered carbocycle; or
  - (v) taken together with A<sub>1</sub> to form a fused 5- to 7-membered carbocycle or heterocycle;
- wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C<sub>1</sub>-C<sub>4</sub>alkyl and haloC<sub>1</sub>-C<sub>4</sub>alkyl;

Each R<sub>4</sub> is independently:

- (i) hydrogen, cyano or C<sub>1</sub>-C<sub>4</sub>alkyl; or
- (ii) taken together with R<sub>3</sub> attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R<sub>b</sub>;

A<sub>1</sub> is N or CR<sub>n</sub>, or A<sub>1</sub> is taken together with a R<sub>3</sub> group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A<sub>2</sub>, A<sub>3</sub>, A<sub>4</sub> and A<sub>5</sub> are independently N or CR<sub>n</sub>;

$R_a$  is independently chosen at each occurrence from hydrogen,  $R_b$  and groups that are taken together with an adjacent  $R_a$  to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from  $R_b$ ; and

$R_b$  is independently chosen at each occurrence from:

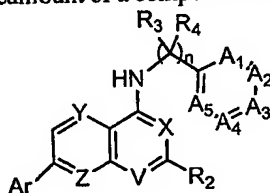
(i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and  $-\text{COOH}$ ; and

(ii)  $\text{C}_1\text{-C}_8$ alkyl,  $\text{C}_1\text{-C}_8$ alkenyl,  $\text{C}_1\text{-C}_8$ alkynyl, halo $\text{C}_1\text{-C}_8$ alkyl,  $\text{C}_1\text{-C}_8$ alkoxy, halo $\text{C}_1\text{-C}_8$ alkoxy,  $\text{C}_1\text{-C}_8$ alkanoyl,  $\text{C}_3\text{-C}_8$ alkanone,  $\text{C}_1\text{-C}_8$ alkanoyloxy,  $\text{C}_1\text{-C}_8$ alkylthio,  $\text{C}_2\text{-C}_8$ alkyl ether,  $\text{C}_1\text{-C}_4$ alkoxycarbonyl,  $\text{C}_1\text{-C}_6$ alkylsulfonyl, mono- and di- $(\text{C}_1\text{-C}_6$ alkyl)aminosulfonyl, and mono- and di- $(\text{C}_1\text{-C}_6$ alkyl)amino $\text{C}_0\text{-C}_4$ alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano,  $\text{C}_1\text{-C}_4$ alkyl,  $\text{C}_1\text{-C}_4$ alkoxy, hydroxy $\text{C}_1\text{-C}_4$ alkyl, halo $\text{C}_1\text{-C}_4$ alkyl, and mono- and di- $(\text{C}_1\text{-C}_4$ alkyl)amino;

and thereby alleviating itch in the patient.

81. A method according to claim 80, wherein the compound is a compound according to claim any one of claims 1-45.

82. A method for treating cough or hiccup in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or  $\text{CR}_{1i}$ , such that at least one of V and X is N;

$R_{1i}$  is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino,  $\text{C}_1\text{-C}_6$ alkyl, halo $\text{C}_1\text{-C}_6$ alkyl,  $\text{C}_1\text{-C}_6$ alkoxy, halo $\text{C}_1\text{-C}_6$ alkoxy and mono- and di- $(\text{C}_1\text{-C}_6$ alkyl)amino;

$R_2$  is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula  $-\text{R}_x\text{-L-M-R}_y$ , wherein:

$\text{R}_x$  is  $\text{C}_0\text{-C}_3$ alkylene;

L is a single covalent bond, O,  $(\text{C}=\text{O})$ ,  $(\text{C}=\text{O})\text{O}$ ,  $\text{O}(\text{C}=\text{O})$ , S,  $\text{SO}_2$ ,  $(\text{C}=\text{O})_p\text{N}(\text{R}_z)$ ,  $\text{N}(\text{R}_z)(\text{C}=\text{O})_p$ ,  $\text{SO}_2\text{N}(\text{R}_z)$  or  $\text{N}(\text{R}_z)\text{SO}_2$ , wherein p is 0 or 1;

M is a single covalent bond,  $\text{C}_1\text{-C}_8$ alkyl,  $\text{C}_1\text{-C}_8$ alkenyl or  $\text{C}_1\text{-C}_8$ alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; and

$R_y$  is:

(a) hydrogen;

- (b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl,  $C_1$ - $C_8$ alkoxy,  $(C_1$ - $C_8$ alkyl)amino,  $C_0$ - $C_8$ alkyl,  $C_1$ - $C_8$ alkanoyl,  $C_2$ - $C_8$ alkanone,  $C_2$ - $C_8$ alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; or
- (c) taken together with  $R_x$  or  $R_z$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

$R_z$  is:

- (a) hydrogen;
- (b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl,  $C_1$ - $C_8$ alkanoyl,  $C_2$ - $C_8$ alkanone,  $C_2$ - $C_8$ alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; or
- (c) taken together with  $R_x$  or  $R_y$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

$n$  is 1, 2 or 3;

Each  $R_3$  is independently:

- (i) chosen from hydrogen, cyano and  $C_1$ - $C_4$ alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
  - (ii) taken together with  $R_4$  attached to the same carbon atom to form an oxo group;
  - (iii) taken together with  $R_4$  attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
  - (iv) taken together with a second  $R_3$  group to form a 3- to 7-membered carbocycle; or
  - (v) taken together with  $A_1$  to form a fused 5- to 7-membered carbocycle or heterocycle;
- wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy,  $C_1$ - $C_4$ alkyl and halo- $C_1$ - $C_4$ alkyl;

Each  $R_4$  is independently:

- (i) hydrogen, cyano or  $C_1$ - $C_4$ alkyl; or
- (ii) taken together with  $R_3$  attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

$A_r$  is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from  $R_b$ ;

$A_1$  is N or  $CR_b$ , or  $A_1$  is taken together with a  $R_3$  group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

$A_2$ ,  $A_3$ ,  $A_4$  and  $A_5$  are independently N or  $CR_b$ ;

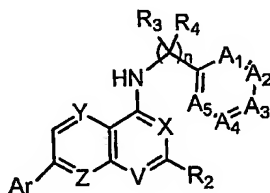
$R_b$  is independently chosen at each occurrence from hydrogen,  $R_b$  and groups that are taken together with an adjacent  $R_a$  to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from  $R_b$ ; and

$R_b$  is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and  $-\text{COOH}$ ;  
and  
(ii)  $\text{C}_1\text{-C}_8$ alkyl,  $\text{C}_1\text{-C}_8$ alkenyl,  $\text{C}_1\text{-C}_8$ alkynyl, halo $\text{C}_1\text{-C}_8$ alkyl,  $\text{C}_1\text{-C}_8$ alkoxy, halo $\text{C}_1\text{-C}_8$ alkoxy,  $\text{C}_1\text{-C}_8$ alkanoyl,  $\text{C}_3\text{-C}_8$ alkanone,  $\text{C}_1\text{-C}_8$ alkanoyloxy,  $\text{C}_1\text{-C}_8$ alkylthio,  $\text{C}_2\text{-C}_8$ alkyl ether,  $\text{C}_1\text{-C}_4$ alkoxycarbonyl,  $\text{C}_1\text{-C}_6$ alkylsulfonyl, mono- and di- $(\text{C}_1\text{-C}_6\text{alkyl})$ aminosulfonyl, and mono- and di- $(\text{C}_1\text{-C}_6\text{alkyl})$ amino $\text{C}_0\text{-C}_4$ alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano,  $\text{C}_1\text{-C}_4$ alkyl,  $\text{C}_1\text{-C}_4$ alkoxy, hydroxy $\text{C}_1\text{-C}_4$ alkyl, halo $\text{C}_1\text{-C}_4$ alkyl, and mono- and di- $(\text{C}_1\text{-C}_4\text{alkyl})$ amino;  
and thereby alleviating cough or hiccup in the patient.

83. A method according to claim 82, wherein the compound is a compound according to claim any one of claims 1-45.

84. A method for treating urinary incontinence or overactive bladder in a patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or  $\text{CR}_1$ , such that at least one of V and X is N;

$\text{R}_1$  is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino,  $\text{C}_1\text{-C}_6$ alkyl, halo $\text{C}_1\text{-C}_6$ alkyl,  $\text{C}_1\text{-C}_6$ alkoxy, halo $\text{C}_1\text{-C}_6$ alkoxy and mono- and di- $(\text{C}_1\text{-C}_6\text{alkyl})$ amino;

$\text{R}_2$  is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula  $-\text{R}_x\text{-L-M-R}_y$ , wherein:

$\text{R}_x$  is  $\text{C}_0\text{-C}_3$ alkylene;

L is a single covalent bond, O,  $(\text{C}=\text{O})$ ,  $(\text{C}=\text{O})\text{O}$ ,  $\text{O}(\text{C}=\text{O})$ , S,  $\text{SO}_2$ ,  $(\text{C}=\text{O})_p\text{N}(\text{R}_2)$ ,  $\text{N}(\text{R}_2)(\text{C}=\text{O})_p$ ,  $\text{SO}_2\text{N}(\text{R}_2)$  or  $\text{N}(\text{R}_2)\text{SO}_2$ , wherein p is 0 or 1;

M is a single covalent bond,  $\text{C}_1\text{-C}_8$ alkyl,  $\text{C}_1\text{-C}_8$ alkenyl or  $\text{C}_1\text{-C}_8$ alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from  $\text{R}_6$ ; and

$\text{R}_y$  is:

(a) hydrogen;

(b)  $\text{C}_1\text{-C}_8$ alkyl,  $\text{C}_2\text{-C}_8$ alkenyl,  $\text{C}_2\text{-C}_8$ alkynyl,  $\text{C}_1\text{-C}_8$ alkoxy,  $(\text{C}_1\text{-C}_8\text{alkyl})$ amino $\text{C}_0\text{-C}_8$ alkyl,  $\text{C}_1\text{-C}_8$ alkanoyl,  $\text{C}_2\text{-C}_8$ alkanone,  $\text{C}_2\text{-C}_8$ alkyl ether, or a 4- to 10-membered

carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; or

- (c) taken together with  $R_x$  or  $R_z$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

$R_z$  is:

- (a) hydrogen;
- (b)  $C_1$ - $C_8$ alkyl,  $C_2$ - $C_8$ alkenyl,  $C_2$ - $C_8$ alkynyl,  $C_1$ - $C_8$ alkanoyl,  $C_2$ - $C_8$ alkanone,  $C_2$ - $C_8$ alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from  $R_b$ ; or
- (c) taken together with  $R_x$  or  $R_y$  to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from  $R_b$ ;

$n$  is 1, 2 or 3;

Each  $R_3$  is independently:

- (i) chosen from hydrogen, cyano and  $C_1$ - $C_4$ alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
  - (ii) taken together with  $R_4$  attached to the same carbon atom to form an oxo group;
  - (iii) taken together with  $R_4$  attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
  - (iv) taken together with a second  $R_3$  group to form a 3- to 7-membered carbocycle; or
  - (v) taken together with  $A_1$  to form a fused 5- to 7-membered carbocycle or heterocycle;
- wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy,  $C_1$ - $C_4$ alkyl and halo $C_1$ - $C_4$ alkyl;

Each  $R_4$  is independently:

- (i) hydrogen, cyano or  $C_1$ - $C_4$ alkyl; or
- (ii) taken together with  $R_3$  attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

$Ar$  is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from  $R_b$ ;

$A_1$  is N or  $CR_a$ , or  $A_1$  is taken together with a  $R_3$  group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

$A_2$ ,  $A_3$ ,  $A_4$  and  $A_5$  are independently N or  $CR_a$ ;

$R_a$  is independently chosen at each occurrence from hydrogen,  $R_b$  and groups that are taken together with an adjacent  $R_a$  to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from  $R_b$ ; and

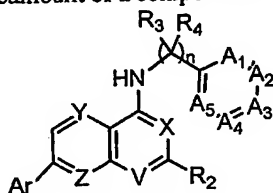
$R_b$  is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and  $-COOH$ ;
- and

(ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl, C<sub>1</sub>-C<sub>8</sub>alkynyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>4</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino; and thereby alleviating urinary incontinence or overactive bladder in the patient.

85. A method according to claim 84, wherein the compound is a compound according to claim any one of claims 1-45.

86. A method promoting weight loss in an obese patient, comprising administering to a patient a therapeutically effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

V, X, Y and Z are each independently N or CR<sub>1</sub>, such that at least one of V and X is N;

R<sub>1</sub> is independently selected at each occurrence from hydrogen, halogen, hydroxy, cyano, amino, C<sub>1</sub>-C<sub>6</sub>alkyl, haloC<sub>1</sub>-C<sub>6</sub>alkyl, C<sub>1</sub>-C<sub>6</sub>alkoxy, haloC<sub>1</sub>-C<sub>6</sub>alkoxy and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)amino;

R<sub>2</sub> is:

(i) hydrogen, halogen, nitro or cyano; or

(ii) a group of the formula -R<sub>x</sub>-L-M-R<sub>y</sub>, wherein:

R<sub>x</sub> is C<sub>0</sub>-C<sub>3</sub>alkylene;

L is a single covalent bond, O, (C=O), (C=O)O, O(C=O), S, SO<sub>2</sub>, (C=O)<sub>p</sub>N(R<sub>2</sub>), N(R<sub>2</sub>)(C=O)<sub>p</sub>, SO<sub>2</sub>N(R<sub>2</sub>) or N(R<sub>2</sub>)SO<sub>2</sub>, wherein p is 0 or 1;

M is a single covalent bond, C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl or C<sub>1</sub>-C<sub>8</sub>alkynyl, wherein each alkyl, alkenyl or alkynyl is substituted with from 0 to 9 substituents independently selected from R<sub>6</sub>; and

R<sub>y</sub> is:

(a) hydrogen;

(b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, (C<sub>1</sub>-C<sub>8</sub>alkyl)aminoC<sub>0</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>6</sub>; or

(c) taken together with R<sub>x</sub> or R<sub>2</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>6</sub>;

R<sub>x</sub> is:

- (a) hydrogen;
- (b) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>2</sub>-C<sub>8</sub>alkenyl, C<sub>2</sub>-C<sub>8</sub>alkynyl, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>2</sub>-C<sub>8</sub>alkanone, C<sub>2</sub>-C<sub>8</sub>alkyl ether, or a 4- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>; or
- (c) taken together with R<sub>x</sub> or R<sub>y</sub> to form a 4- to 10-membered carbocycle or heterocycle that is substituted with from 0 to 9 substituents independently selected from R<sub>b</sub>;

n is 1, 2 or 3;

Each R<sub>3</sub> is independently:

- (i) chosen from hydrogen, cyano and C<sub>1</sub>-C<sub>4</sub>alkyl that is substituted with from 0 to 3 substituents independently chosen from halogen, cyano and hydroxy;
- (ii) taken together with R<sub>4</sub> attached to the same carbon atom to form an oxo group;
- (iii) taken together with R<sub>4</sub> attached to the same carbon atom to form a 3- to 6-membered carbocycle or heterocycle;
- (iv) taken together with a second R<sub>3</sub> group to form a 3- to 7-membered carbocycle; or
- (v) taken together with A<sub>1</sub> to form a fused 5- to 7-membered carbocycle or heterocycle; wherein each of (iii), (iv) and (v) is substituted with from 0 to 3 substituents independently chosen from halogen, cyano, hydroxy, C<sub>1</sub>-C<sub>4</sub>alkyl and haloC<sub>1</sub>-C<sub>4</sub>alkyl;

Each R<sub>4</sub> is independently:

- (i) hydrogen, cyano or C<sub>1</sub>-C<sub>4</sub>alkyl; or
- (ii) taken together with R<sub>3</sub> attached to the same carbon atom to form an oxo group or an optionally substituted 3- to 6-membered carbocycle or heterocycle;

Ar is a 5- to 10-membered carbocycle or heterocycle, each of which is substituted with from 0 to 3 substituents independently selected from R<sub>b</sub>;

A<sub>1</sub> is N or CR<sub>a</sub>, or A<sub>1</sub> is taken together with a R<sub>3</sub> group to form an optionally substituted, fused, 5- to 7-membered carbocycle or heterocycle;

A<sub>2</sub>, A<sub>3</sub>, A<sub>4</sub> and A<sub>5</sub> are independently N or CR<sub>a</sub>;

R<sub>a</sub> is independently chosen at each occurrence from hydrogen, R<sub>b</sub> and groups that are taken together with an adjacent R<sub>a</sub> to form a fused 5- or 6-membered carbocyclic or heterocyclic ring that is substituted with from 0 to 4 substituents independently chosen from R<sub>b</sub>; and

R<sub>b</sub> is independently chosen at each occurrence from:

- (i) hydrogen, hydroxy, halogen, amino, aminocarbonyl, aminosulfonyl, cyano, nitro and -COOH; and
- (ii) C<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkenyl, C<sub>1</sub>-C<sub>8</sub>alkynyl, haloC<sub>1</sub>-C<sub>8</sub>alkyl, C<sub>1</sub>-C<sub>8</sub>alkoxy, haloC<sub>1</sub>-C<sub>8</sub>alkoxy, C<sub>1</sub>-C<sub>8</sub>alkanoyl, C<sub>3</sub>-C<sub>8</sub>alkanone, C<sub>1</sub>-C<sub>8</sub>alkanoyloxy, C<sub>1</sub>-C<sub>8</sub>alkylthio, C<sub>2</sub>-C<sub>8</sub>alkyl ether, C<sub>1</sub>-C<sub>4</sub>alkoxycarbonyl, C<sub>1</sub>-C<sub>6</sub>alkylsulfonyl, mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminosulfonyl, and mono- and di-(C<sub>1</sub>-C<sub>6</sub>alkyl)aminoC<sub>0</sub>-C<sub>4</sub>alkyl; each of which is substituted with from 0 to 3

substituents independently chosen from hydroxy, halogen, amino, cyano, C<sub>1</sub>-C<sub>4</sub>alkyl, C<sub>1</sub>-C<sub>4</sub>alkoxy, hydroxyC<sub>1</sub>-C<sub>4</sub>alkyl, haloC<sub>1</sub>-C<sub>4</sub>alkyl, and mono- and di-(C<sub>1</sub>-C<sub>4</sub>alkyl)amino; and thereby promoting weight loss in the patient.

87. A method according to claim 86, wherein the compound is a compound according to claim any one of claims 1-45.

88. A compound or salt according to any one of claims 1-45, wherein the compound or salt is radiolabeled.

89. A method for determining the presence or absence of capsaicin receptor in a sample, comprising the steps of:

- (a) contacting a sample with a compound or salt according to any one of claims 1-45, under conditions that permit binding of the compound to capsaicin receptor; and
- (b) detecting a level of the compound bound to capsaicin receptor, and therefrom determining the presence or absence of capsaicin receptor in the sample.

90. A method according to claim 89, wherein the compound is a radiolabeled compound according to claim 88, and wherein the step of detection comprises the steps of:

- (i) separating unbound compound from bound compound; and
- (ii) detecting the presence or absence of bound compound in the sample.

91. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 49 in a container; and
- (b) instructions for using the composition to treat pain.

92. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 49 in a container; and
- (b) instructions for using the composition to treat cough or hiccup.

93. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 49 in a container; and
- (b) instructions for using the composition to treat obesity.

94. A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 49 in a container; and
- (b) instructions for using the composition to treat urinary incontinence or overactive bladder.

95. The use of a compound or salt according to any one of claims 1-45 for the manufacture of a medicament for the treatment of a condition responsive to capsaicin receptor modulation.



96. A use according to claim 95, wherein the condition is pain, asthma, chronic obstructive pulmonary disease, cough, hiccup, obesity, urinary incontinence, overactive bladder, exposure to capsaicin, burn or irritation due to exposure to heat, burn or irritation due to exposure to light, burn, bronchoconstriction or irritation due to exposure to tear gas, infectious agent, air pollutants or pepper spray, or burn or irritation due to exposure to acid.